

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

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|---|---|
| Date of mailing (day/month/year) 25 June 2001 (25.06.01) | To: Commissioner US Department of Commerce United States Patent and Trademark Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 ETATS-UNIS D'AMERIQUE in its capacity as elected Office |
| International application No. PCT/US00/15783 | Applicant's or agent's file reference RUTC 99-0048 |
| International filing date (day/month/year) 08 June 2000 (08.06.00) | Priority date (day/month/year) 08 June 1999 (08.06.99) |
| Applicant LAM, Eric | |

1. The designated Office is hereby notified of its election made:

 in the demand filed with the International Preliminary Examining Authority on:

05 January 2001 (05.01.01)

 in a notice effecting later election filed with the International Bureau on:

2. The election was was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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|---|--|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 | Authorized officer Antonia Muller Telephone No.: (41-22) 338.83.38 |
|---|--|

PATENT COOPERATION TREATY

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NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

| | |
|---|--|
| Date of mailing (day/month/year) 22 November 2001 (22.11.01) | From the INTERNATIONAL BUREAU To: LICATA, Jane, Massey Licata & Tyrrell P.C. 66 E. Main Street Marlton, NJ 08053 ETATS-UNIS D'AMERIQUE |
| Applicant's or agent's file reference RU-0167 | IMPORTANT NOTIFICATION |
| International application No. PCT/US00/15783 | International filing date (day/month/year) 08 June 2000 (08.06.00) |

1. The following indications appeared on record concerning:

the applicant the inventor the agent the common representative

| | | |
|--|----------------------------|--------------------------|
| Name and Address RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY Old Queens Somerset Street New Brunswick, NJ 08903 United States of America | State of Nationality US | State of Residence US |
| Telephone No. | | |
| Facsimile No. | | |
| Teleprinter No. | | |

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person the name the address the nationality the residence

| | | |
|---|----------------------------|--------------------------|
| Name and Address RUTGERS, THE STATE UNIVERSITY Old Queens Somerset Street New Brunswick, NJ 08903 United States of America | State of Nationality US | State of Residence US |
| Telephone No. | | |
| Facsimile No. | | |
| Teleprinter No. | | |

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

the receiving Office the designated Offices concerned
 the International Searching Authority the elected Offices concerned
 the International Preliminary Examining Authority other:

| | |
|---|--|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 | Authorized officer Simin Baharlou Telephone No.: (41-22) 338.83.38 |
|---|--|

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JANE MASSEY LICATA
LICATA & TYRRELL P.C.
66 E MAIN STREET
MARLTON, NEW JERSEY 08053

NP: 12/8/01

RECEIVED
OCT 25 2001
PCT

NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing
(day/month/year)

23 OCT 2001

Applicant's or agent's file reference
RUTC 99-0048

IMPORTANT NOTIFICATION

International application No.
PCT/US00/15783International filing date (day/month/year)
06 JUNE 2000Priority Date (day/month/year)
NONEApplicant
RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB.301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

ASHWIN MEHTA

Telephone No. (703) 305-0196

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference RUTC 99-0048 | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No. PCT/US00/15783 | International filing date (day/month/year) 08 JUNE 2000 | Priority date (day/month/year) NONE |
| International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet. | | |
| Applicant RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

| | |
|--|--|
| Date of submission of the demand 05 JANUARY 2001 | Date of completion of this report 14 SEPTEMBER 2001 |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 | Authorized officer <i>Jaypee Bridgers</i> ASHWIN MEHTA |
| Facsimile No. (703) 305-8230 | Telephone No. (703) 305-0196 |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15783

I. Basis of the report

1. With regard to the elements of the international application:*

 the international application as originally filed the description:

pages 1-27

pages NONE

pages NONE

, filed with the letter of

 the claims:

pages 28-34

pages NONE, as amended (together with any statement) under Article 19

pages NONE

pages NONE

, filed with the letter of

 the drawings:

pages 1-2

pages NONE, as originally filed

pages NONE

pages NONE

, filed with the letter of

 the sequence listing part of the description:

pages NONE

pages NONE, as originally filed

pages NONE

pages NONE

, filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. The amendments have resulted in the cancellation of: the description, pages NONE the claims, Nos. NONE the drawings, sheets/fig NONE5. This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15783

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

| | | | |
|-------------------------------|--------|------|-----|
| Novelty (N) | Claims | 1-32 | YES |
| | Claims | NONE | NO |
| Inventive Step (IS) | Claims | NONE | YES |
| | Claims | 1-32 | NO |
| Industrial Applicability (IA) | Claims | 1-32 | YES |
| | Claims | NONE | NO |

2. citations and explanations (Rule 70.7)

Claims 1-32 lack an inventive step under PCT Article 33(3) as being obvious over Kempin et al in view of Llyznik et al and Miao et al.

Kempin et al teach a method to target insertions into pre-determined locations in a genome via homologous recombination and regeneration of transgenic plants (pages 802-805).

Kempin et al do not teach use of a site-specific recombination system to remove genes from the target site.

Llyznik et al teach use of a site-specific recombination system to remove marker genes previously inserted into a genome (pages 3786-3787).

Miao et al teach method to target insertions into pre-determined locations in a genome and suggest the application of negative selectable marker genes such as cytosine deaminase with the system (pages 360-363).

It would have been obvious and within the scope of one of ordinary skill in the art to modify the method of homologous recombination-mediated targeted insertion of Kempin et al by using negative selection marker genes, as suggested by Miao et al. One may flank the marker gene with substrate sites for a site-specific recombinase to facilitate its removal, as taught by Llyznik et al, following selection of transformed plants. One may include a selectable marker gene in the transformation construct, such that the target sequence is located between the promoter and the coding region, as taught by Llyznik et al. This configuration would obviously aid in screening for primary transformants, as well as in screening for the homologous recombination event. One would be motivated to include further positive and selectable marker genes in the construct of Kempin et al, given the suggestion by Miao et al. One would also obviously be motivated to use other types of positive and negative selection marker genes, such as the hpt gene of Llyznik et al, as is suitable for a particular application of the method.

Claims 1-32 meet the criteria set out in PCT Article 33(2) and (4), because the prior art does not teach nucleic acid constructs useful for homologous recombination for targeted gene insertion, and comprising substrate sites for site-specific recombinases. (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/15783

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 21 and 30 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: the recitation "the one of the DNA substrates" is objected to. The recitation is awkward, and grammatically incorrect. The word "the" should be removed from the recitation.

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): C12N 5/04, 15/09, 15/63, 15/65, 15/82, 15/84, 15/87; A01H 1/00, 5/00, 5/10 and US Cl: 435/69.1, 320.1, 410, 419, 468, 469; 800/278, 287, 288, 295, 298

V. 2. REASoNED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

The claims meet the industrial applicability of being useful for insertion of agronomically important genes into food crops.

----- NEW CITATIONS -----KEMPIN et al. Targeted Disruption In *Arabidopsis*. *Nature*. 23 October 1997, Vol. 389, pages 802-803, see whole document.LYZNIK et al. FLP-Mediated Recombination Of FRT Sites In The Maize Genome. *Nucl. Acids Res.* 1996, Vol. 24, No. 19, pages 3784-3789, see pages 3784-3787.MIAO et al. Targeted Disruption Of The TGA3 Locus In *Arabidopsis thaliana*. *Plant J.* 1995, Vol. 7, No. 2, pages 359-365, see whole document.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15783

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12N 5/04, 15/09, 15/63, 15/65, 15/82, 15/84, 15/87; A01H 1/00, 5/00, 5/10
US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 320.1, 410, 419, 468, 469; 800/278, 287, 288, 295, 298

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST, AGRICOLA CAPLUS, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| Y | SMITH et al. Characterization And Mapping Of Ds-GUS-T-DNA Lines For Targeted Insertional Mutagenesis. Plant J. 1996, Vol. 10, No. 4, pages 721-732, especially pages 722-726, 728, 730, 731. | 1-32 |
| Y | SUNDARESAN et al. Patterns Of Gene Action In Plant Development Revealed By Enhancer Trap And Gene Trap Transposable Elements. Genes Dev. 1995, Vol. 9, pages 1797-1810, especially pages 1798-1803. | 1-32 |
| Y | ENOKI et al. Ac As A Tool For The Functional Genomics Of Rice. Plant J. 1999, Vol. 19, No. 5, pages 605-613, especially pages 610-612. | 1-32 |
| — | | — |
| A | | 1-32 |
| Y | WO 92/01370 A1 (REGENT OF THE UNIVERSITY OF CALIFORNIA) 06 February 1992, page 24, line 31 to page 36, line 15. | 1-32 |

 Further documents are listed in the continuation of Box C. See patent family annex.

| | | | |
|-----|---|------|--|
| • | Special categories of cited documents: | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| •A* | document defining the general state of the art which is not considered to be of particular relevance | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| •B* | earlier document published on or after the international filing date | "Y" | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| •L* | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "g." | document member of the same patent family |
| •O* | document referring to an oral disclosure, use, exhibition or other means | | |
| •P* | document published prior to the international filing date but later than the priority date claimed | | |

Date of the actual completion of the international search

23 AUGUST 2000

Date of mailing of the international search report

18 SEP 2000

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703) 305-3230

Authorized officer

ASHWIN MEHTA

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15783

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

435/69.1, 320.1, 410, 419, 468, 469; 800/278, 287, 288, 295, 298